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UNITED STATES DISTRICT COURT

SOUTHERN DISTRICT OF CALIFORNIA

GEN-PROBE, INCORPORATED,

Plaintiff,

v.

VYSIS, INC.,

Defendant.

CASE NO. 99CV 2668H (AJB)

VYSIS' OPPOSITION TO GEN-PROBE'S MOTION FOR PARTIAL SUMMARY JUDGMENT OF NONINFRINGEMENT UNDER THE DOCTRINE OF EQUIVALENTS

Date: November 13, 2001
Time: 10:30 a.m.
Place: Courtroom 1

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I. INTRODUCTION

Gen-Probe's motion is rife with factual assertions concerning the purported substantiality of the differences between its transcription-mediated amplification ("TMA") technique and the amplification protocols within the scope of the claims of Vysis' United States Patent No. 5,750,338 ("the '338 patent"), as currently interpreted by the Court.[1] As discussed below, the parties strongly dispute those facts. Further, finding that TMA is equivalent to the amplification techniques within the scope of the '338 patent is fully consistent with the "all elements" rule. Accordingly, summary judgment in favor of Gen-Probe on the issue of infringement under the doctrine of equivalents is improper.

II. THE COURT SHOULD DEFER RESOLUTION OF GEN-PROBE'S MOTION PENDING THE DEPOSITIONS OF GEN-PROBE'S EXPERTS

Gen-Probe's motion presents an extensive factual discussion concerning the purported differences between its TMA amplification technique and the amplification techniques within the scope of the claims of the '338 patent. Gen-Probe bases those factual assertions on the declaration of Dr. Kary B. Mullis, who has been retained by Gen-Probe as a testifying expert in this case. Gen-Probe has previously submitted an expert report from Dr. Mullis, as well as an expert report from Dr. Michael Harpold. Both of those expert reports contain significant discussions of the views of those experts on the issue of equivalence between TMA and the amplification techniques of the '338 patent.

The depositions of Gen-Probe's experts on the doctrine of equivalents issue are scheduled to take place after this Opposition will be filed with the Court.[2] Vysis cannot adequately oppose Gen-Probe's motion until it has had an opportunity to examine Dr. Mullis and Dr. Harpold about their opinions on the very issues that are the subject of Gen-Probe's motion. At a minimum, Vysis should

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[1] By order entered June 20, 2001, this Court construed the claims of the '338 patent as literally encompassing only non-specific amplification. Vysis contends that that ruling was incorrect as a matter of law. References herein to the literal scope of the '338 patent claims are to the Court's construction of those claims.

[2] Gen-Probe's motion was filed on October 16, 2001, and this Opposition is due on October 30, 2001. Dr. Mullis is scheduled for deposition on November 2, 2001, and Dr. Harpold is scheduled for deposition on November 14, 2001.

be permitted to depose Dr. Mullis concerning his Declaration that accompanied Gen-Probe's motion prior to having to respond substantively to the motion.

Accordingly, Gen-Probe's motion should be continued, pursuant to Fed. R. Civ. P. 56(f), until after Vysis has taken discovery of the expert witnesses Gen-Probe relies upon to support the factual assertions that underlie its motion. Until that discovery is taken, Vysis cannot fully respond to Gen-Probe's motion. The remainder of this Opposition sets forth the limited response Vysis is able to provide at this time, and Vysis requests an opportunity to supplement this Opposition with material developed through discovery of Gen-Probe's experts.

III. WHETHER GEN-PROBE'S TMA IS SUBSTANTIALLY DIFFERENT FROM THE AMPLIFICATION TECHNIQUES CLAIMED IN THE '338 PATENT RAISES GENUINE ISSUES OF MATERIAL FACT

Infringement under the doctrine of equivalents is a question of fact. *Insituform Techs., Inc. v. Cat Contracting, Inc.*, 161 F.3d 688, 692 (Fed. Cir. 1998). Summary judgment of noninfringement under the doctrine of equivalents is improper because a reasonable factfinder can find the differences between the allegedly infringing product and the claimed invention are insubstantial. *See Optical Disc Corp. v. Del Mar Avionics*, 208 F.3d 1324, 1336-37 (Fed. Cir. 2000). As described below, there is a very real factual dispute regarding the purported differences between the amplification techniques within the literal scope of the claims of the '338 patent and the amplification technique used in Gen-Probe's HIV/HCV test.[3] That factual dispute precludes granting summary judgment to Gen-Probe.

Each claim of the '338 patent includes an element of "amplifying" a target polynucleotide. Gen-Probe's HIV/HCV test performs the amplification step recited in the '338 patent by a technique it calls "transcription-mediated amplification," or "TMA." The TMA process serves to increase the number of polynucleotides in the tested sample. As discussed in detail in the accompanying Declaration of David H. Persing, M.D., Ph.D. ("Persing Decl."), TMA performs substantially the same function, in substantially the same way, to achieve substantially the same result as the

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[3] Apart from the amplification element of the claims of the '338 patent, Gen-Probe does not rely upon any other grounds for noninfringement for the purposes of its motion. (Memorandum of (continued...)

amplification methods that the Court has held are within the literal scope of the claims of the '338 patent.[4]

Contrary to Gen-Probe's portrayal, no bright line can be drawn between "specific" and "non-specific" amplification techniques. Indeed, all nucleic acid amplification techniques have some element of non-specificity. (Persing Decl., ¶ 6.) Even the methods Gen-Probe calls "specific" protocols, such as polymerase chain reaction ("PCR") amplification and TMA, are non-specific to varying degrees. (*Id.*) The degree of nonspecificity of an amplification protocol depends on the conditions of amplification and the intrinsic properties of the protocol. (*Id.*) Accordingly, it is improper to characterize a particular amplification protocol as completely "specific" or completely "non-specific."[5]

Moreover, equivalence of the amplification step of the claims of the '338 patent and the TMA step of Gen-Probe's HIV/HCV test must be viewed in the context of the claimed invention. *See Warner-Jenkinson Co. v. Hilton-Davis Chem. Co.*, 520 U.S. 17, 40 (1997) ("An analysis of the role played by each element in the context of the specific patent claim will thus inform the inquiry as to whether a substitute element matches the function, way, and result of the claimed element, or whether the substitute element plays a role substantially different from the claimed element."). The claims of the '338 patent are not directed solely to amplification of polynucleotides. Rather, they recite a process for contacting a sample with a support which binds to the target polynucleotide, separating the support and bound target from the remainder of the sample, and then amplifying the

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(...continued)
Points and Authorities of Plaintiff Gen-Probe Incorporated in Support of its Motion for Partial Summary Judgment of Non-Infringement of Equivalents [sic] ("G-P Mem.") at 2 n.3.)

[4] As Gen-Probe acknowledges, the Supreme Court has noted that the "triple identity" test may be unsuitable in determining the equivalence of process claims. (G-P Mem. at 16 n.10.) However, even under that test (which examines whether the accused product performs *substantially* the same function, in *substantially* the same way, to achieve *substantially* the same result), Gen-Probe's HIV/HCV test is equivalent to the claims of the '338 patent.

[5] Further, Gen-Probe's arguments largely rest upon generalized differentiations between "specific" and "non-specific" techniques. (See G-P Mem. at 17-18.) That is not the appropriate analysis for this case. Rather, the correct analysis is whether an element of the *accused product* (Gen-Probe's TMA technique) is equivalent to an element of the *claimed invention* (the amplification step of the claims of the '338 patent). *See Warner-Jenkinson Co. v. Hilton-Davis Chem. Co.*, 520 U.S. 17, 43-44 (1997).

target.[6] The separation step present in the claims assures that no non-target polynucleotides will be present when the amplification step is performed. When viewed in this context, Gen-Probe's numerous assertions regarding the purported differences between "non-specific" amplification and TMA become irrelevant.

The purpose of the amplification step of the multi-step process claimed in the '338 patent is to increase the amount of target polynucleotide after that target has been isolated from the remainder of the sample. Gen-Probe's TMA process performs precisely that function. That process permits detection of the presence of a target polynucleotide that may otherwise go undetected as a result of its low concentration in a clinical sample. (Persing Decl., ¶ 7.)

TMA works by creating a double-stranded DNA molecule from a single-stranded target polynucleotide. (Persing Decl., ¶ 8.) The TMA technique, across several amplification cycles, then uses RNA polymerase to create multiple RNA molecules from that double-stranded DNA. (*Id.*) Those RNA molecules are then detected by contacting them with a complementary labeled DNA probe. (*Id.*)

The TMA process performs in substantially the same way as the amplification techniques disclosed and claimed in the '338 patent. The insubstantial differences can be illustrated by comparing TMA with one of the amplification techniques described in the '338 patent, set forth as Example 5 of the patent. ('338 patent, col. 31, lines 24 - 54.) That example teaches the creation of a double-stranded DNA molecule from a single-stranded target polynucleotide. Example 5 then teaches the use of RNA polymerase to create multiple RNA molecules from that double-stranded DNA. As in Gen-Probe's TMA process, those RNA molecules are detected by contacting them with a complementary labeled DNA probe. (Persing Decl., ¶ 9.)

From a practical perspective, in the context of the claimed invention, the differences between Gen-Probe's TMA technique and the techniques disclosed and claimed in the '338 patent are insignificant. For example, the target polynucleotide of the TMA process may be RNA or DNA. (Persing Decl., ¶ 10.) Indeed, Gen-Probe touts its TMA process as able to use either RNA or DNA

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[6] The first two steps of that process are commonly known as "target capture."

as a target. (See Hill, "Gen-Probe Transcription-Mediated Amplification: System Principles" (attached as Exhibit A to Declaration of L. Scott Burwell in Opposition to Gen-Probe's Motion For Partial Summary Judgment Of Noninfringement Under the Doctrine of Equivalents ("Burwell Decl.")).) Example 5 of the '338 patent uses single-stranded DNA as a target. From a practical standpoint, there is no substantial difference between these targets. (Persing Decl., ¶ 10.) Both are used as templates for the creation of double-stranded DNA, which is then used in both processes to create RNA polynucleotides. (*Id.*)

Another difference between Gen-Probe's TMA process and the amplification process disclosed in Example 5 of the '338 patent, the use of different primers, is not a substantial difference. (*Id.*) Gen-Probe's TMA process uses "specific" primers – that is, primers that have a nucleotide sequence that has been pre-selected to bind with the target polynucleotide at a predetermined sequence. (Persing Decl., ¶ 11.) Two "specific" primers are used in the TMA process. (*Id.*) These primers are used as a "starting point" for the enzyme that creates the double-stranded DNA molecule. (*Id.*)

Example 5 of the '338 patent also uses primers. These primers act in the same way as the primers of the TMA technique – they bind to the target polynucleotide and act as the "starting point" for the enzyme that creates the double-stranded DNA molecule. (Persing Decl., ¶ 12.) While Example 5 refers to "random" primers, and most "random" primers do not bind to a predetermined sequence of the target polynucleotide, this difference is inconsequential in the context of the claimed invention. At least some of the random primers bind to the target in a sequence-specific fashion, thus initiating nucleic acid synthesis. (Persing Decl., ¶ 13.) As long as a double-stranded DNA molecule is created, the particular location of the target polynucleotide to which the primers bind is not important. (*Id.*) Because the target capture step disclosed and claimed in the '338 patent acts to eliminate polynucleotides other than the target, "random" primers will bind only to the target polynucleotide. (*Id.*)

Accordingly, the same result – creation of double-stranded DNA – is reached whether one uses "specific" primers or "random" primers. Indeed, one could use the "specific" primers of Gen-Probe's TMA process in place of the "random" primers of Example 5 and achieve exactly the same

result. (Persing Decl., ¶ 14.) The amplification techniques of the '338 patent will work regardless of whether the primers are called "specific" or "random." (*Id.*)

One of the "specific" primers used in Gen-Probe's TMA technique also contains a "promoter" sequence. (Persing Decl., ¶ 15.) This "promoter" sequence is recognized by the RNA polymerase enzyme, which creates RNA molecules from the double-stranded DNA. (*Id.*) The "promoter" sequence tells the RNA polymerase where to begin transcription of the RNA molecules. (*Id.*) The amplification process of Example 5 also uses an RNA polymerase, but does not require a "promoter" sequence to begin work, as that RNA polymerase has been modified by removing the "sigma subunit." (Persing Decl., ¶ 16.) This modified RNA polymerase allows RNA transcription to begin from any point along the double-stranded DNA molecule. Again, however, the result of the two processes is the same – RNA molecules are transcribed from the double-stranded DNA molecules. (*Id.*)

Accordingly, although the particular biochemical nuances of the amplification protocols described in the '338 patent may differ from those used in Gen-Probe's TMA process, TMA is not *substantially* different from those techniques in the context of the claimed invention. Thus, the amplification step of Gen-Probe's HIV/HCV test is equivalent to the amplification step recited in the claims of the '338 patent.

IV. FINDING EQUIVALENCE WOULD NOT VIOLATE THE "ALL ELEMENTS" RULE

Contrary to Gen-Probe's assertions, a finding that Gen-Probe's TMA technique is equivalent to the amplification step claimed in the '338 patent would not violate the "all elements" rule because it would not vitiate a limitation of the claims.

Gen-Probe argues that "the doctrine of equivalents cannot cover a product or process that encompasses an element that is clearly excluded from the literal terms of a claim." (G-P Mem. at 12.) Yet in this case, specific amplification techniques are *not* "clearly excluded" from the literal terms of the claim.[7] As discussed at length in Vysis' Opposition to Gen-Probe's Motion for Partial

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[7] Vysis is aware of the Court's construction of the term "amplifying" as encompassing only non-specific amplification. Vysis understands, however, that the Court's Order granting partial (continued...)

Summary Judgment on the issue of literal infringement, the specification and prosecution history of the '338 patent do not limit the claims to methods using non-specific amplification.

Gen-Probe asks this Court to deny Vysis the equitable protections afforded by the doctrine of equivalents based on an argument that limitations not specifically recited in the claims and expressly contrary to the prosecution history of the '338 patent would be vitiated by application of the doctrine. That would be a highly inequitable result. Indeed, the Court's prior ruling on the literal scope of the '338 patent claims should be reconsidered, particularly in light of the ongoing clarification of the applicable law resulting from recent decisions of the Federal Circuit and in view of additional information regarding the significance of certain elements of the disclosure of the '338 patent.

Regarding the law, this Court read into the language of the '338 patent claims a requirement for "specific" amplification that simply does not appear in the claims of the patent based on expressed preferences in the text of the patent specification. The Federal Circuit has now made clear that it is legally improper to do so. *Dayco Prods., Inc. v. Total Containment, Inc.*, 258 F.3d 1317, 1327 (Fed. Cir. 2001) (vacating summary judgment of noninfringement).

The Federal Circuit reiterated the impropriety of reading limitations into the claims in vacating a grant of summary judgment of noninfringement in *Gart v. Logitech, Inc.*, 254 F.3d 1334 (Fed. Cir. 2001). In *Gart*, the Federal Circuit held that the district court had improperly added to the claims a limitation appearing in the specification and the drawings, but not appearing in the unambiguous language of the claim. *Id.* at 1342-43. The facts of *Gart* are strikingly similar to the facts of this case. In *Gart*, the district court had interpreted the term "angular medial surface" of the claimed computer mouse invention to require a "ledge" for supporting the user's fingers. In support of that construction, the alleged infringer argued that all of the drawings of the patent showed the claimed support structure as having a ledge, and that the written description described the invention as having a ledge.

(...continued)
summary judgment of noninfringement is not a final judgment, and is therefore subject to revision at any time under Fed. R. Civ. P. 54(b). Vysis believes that Order was based on an error in claim construction, and takes this opportunity to explain why that Order should be revised.

The Federal Circuit rejected the district court's limited claim construction, noting that the specification of the patent did not describe "the invention" as having a ledge. *Id.* at 1342. Further, although it realized that the drawings showed a computer mouse having a ledge, the court realized that the drawings were not "meant to represent 'the' invention or to limit the scope of coverage defined by the words used in the claims themselves," and that the written description did not explicitly limit the subject matter of the patent to the ledge configuration set forth in the drawings. *Id.* The court held that the scope of the claim could be ascertained from the plain language of the claim, and that construing the claim as the district court had would improperly add a limitation from the specification and drawings into the claim. *Id* at 1342-33.

In *Gart*, the Federal Circuit vacated a narrow claim construction that the district court had made based on reasoning very similar to that employed by the Court in this case. As discussed above, the specification of the '338 patent does not explicitly limit the subject matter of the patent to non-specific amplification techniques. Similarly, although the drawings depict the use of non-specific amplification techniques, nothing in those drawings or the accompanying written description limits "the invention" to the techniques described in the drawings. As in *Gart*, the scope of the claims of the '338 patent can be ascertained from the plain language of the claim. Clearly, the plain meaning of the term "amplification" in the context of the '338 patent includes both specific and non-specific techniques.

Another recent case in which the Federal Circuit vacated a district court's narrow claim construction is *Interactive Gift Express, Inc., v. Compuserve Inc.*, 256 F.3d 1323 (Fed. Cir. 2001). In *Interactive Gift Express*, the court found that the district court had read limitations into five separate claim terms. The district court's error in construing one of the terms is particularly instructive to this case. The patent at issue in *Interactive Gift Express* was directed to a system for reproducing information in material objects at point of sale locations. The district court had construed the term "point of sale location" as excluding a home, noting that the specification of the patent explicitly and repeatedly referred to a "point of sale location" as a "retail outlet." *Interactive Gift Express, Inc., v. Compuserve Inc.*, 47 U.S.P.Q.2d 1797, 1805-06 (S.D.N.Y. 1998). The district court further found

that the word "home" did not appear in any of the disclosed embodiments of the patent, and that the sole reference to a "home" was in a section of the specification describing the prior art. *Id.*

The Federal Circuit rejected the district court's narrow construction. First, the Federal Circuit examined the claim language itself, and found nothing *precluding* a home from being a point of sale location. The court first noted that the claims were merely "silent" regarding the possible venues of a point of sale location. *Interactive Gift Express*, 256 F.3d. at 1333. Then, the court looked to the specification. Though the court "acknowledge[d] the great likelihood that a point of sale location will not be a home," the court nonetheless found that the specification did not *preclude* a home from serving as a point of sale location, and that the specification described an embodiment that *could* be utilized in a home.[8] *Id.* at 1333-34. Based on the permissive language of the specification, the court found that the intrinsic evidence unambiguously allowed a home to serve as a point of sale location.[9] *Id.* at 1334.

The Federal Circuit's analysis in *Interactive Gift Express* is directly applicable to the facts of this case. As discussed below, the specification of the '338 patent uses *permissive* language with respect to non-specific amplification techniques, and not *mandatory* language. Thus, the specification does not *preclude* the use of specific amplification techniques in the claimed invention. That the words "specific amplification" or "PCR" do not appear in the specification of the patent is of no matter, as neither the specification or the claims precludes using specific amplification protocols. Just as the district court improperly read the term "point of sale location" as excluding a "home" in *Interactive Gift Express*, so did this Court improperly read the term "amplifying" as excluding non-specific amplification techniques.

There is also additional factual information that has become available since the Court's June 20, 2001 Order. Ongoing discovery has confirmed the correctness of Dr. Persing's testimony that Example 5 of the '338 patent, in which the capture probe may be used as the primer, describes

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[8] The Federal Circuit found that it was possible to use the disclosed embodiment in a home notwithstanding the fact that use in a home was not explicitly contemplated by the specification, and that the word "home" was not even mentioned in the description of the embodiment.

specific amplification. (See May 25, 2001 Declaration of David H. Persing, M.D., Ph.D. filed in Support of Vysis' Opposition to Gen-Probe's Motion for Partial Summary Judgment ("May 25, 2001 Persing Decl."), ¶ 13.) Years after the application for the '338 patent was filed, Gen-Probe's Chief Scientific Officer, Dr. Kacian, proposed in one of his notebooks an amplification scheme similar to that described in Example 5 of the '338 patent in which the capture probe was used as a primer. (See GP-033873, attached as Burwell Decl. Exhibit C.) That this is a specific rather than a non-specific amplification scheme is clear from Dr. Kacian's deposition testimony that none of the amplification schemes he proposed while at Gen-Probe was a non-specific amplification scheme. (Kacian Dep. at 202-203, attached as Burwell Decl. Exhibit B.)

Moreover, Gen-Probe itself acknowledged that the '338 patent claims literally encompass specific amplification in the ongoing reissue proceedings in connection with the '338 patent. There, Gen-Probe alleged that the '338 patent claims were invalid under 35 U.S.C. § 102 because they were *anticipated* by, i.e., lacked novelty in view of, a publication by Powell (attached as Burwell Decl. Exhibit D) that disclosed *only* specific amplification via PCR. Gen-Probe could not have done so if the patent claims did not literally encompass specific amplification.

Accordingly, in view of the new law and facts discussed above, the Court should revisit its prior claim construction and hold that specific amplification techniques are within the scope of the claims of the '338 patent.

A. The '338 Patent Specification Does Not Exclude Specific Amplification Techniques

The primary discussion of the invention of combining target capture with amplification begins at column 30, line 15 of the '338 patent specification. The invention is first defined broadly by the statement that "[t]he sensitivity of the above DNA or RNA target capture methods can be enhanced by **amplifying** the captured nucleic acids." (Emphasis added.) The specification then describes a particular benefit of the invention, that "[t]his **can be** achieved by non-specific replication using standard enzymes . . . ." (Emphasis added.) The specification does **not** say that

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(...continued)

[9] The court further held that the lack of ambiguity made it unnecessary to address any of the (continued...)

enhanced sensitivity of the target capture methods **is** achieved by non-specific amplification, but rather uses **permissive** language, i.e., that enhanced sensitivity **can be** achieved by non-specific amplification.

The specification then again describes the invention as including amplification generally in the paragraph at column 30, lines 23-29. The paragraph following this describes both specific and non-specific amplification, but points out the particular benefits of the invention when using non-specific amplification:

> Amplification of the target nucleic acid sequences, because it follows purification of the target sequences, **can** employ non-specific enzymes or printers (i.e. enzymes or primers which are capable of causing the replication of virtually any nucleic acid sequence). Although any background, non-target, nucleic acids are replicated along with target, this is not a problem because most of the background nucleic acids have been removed in the course of the capture process. Thus **no specially tailored primers are *needed*** for each test, and the same standard amplification reagents can be used, regardless of the targets.

Col. 30, lines 30-40 (emphasis added).

The reference to "specially tailored primers" is an explicit reference to specific amplification techniques. The specification does not say that such specific techniques cannot be used. Rather, the '338 specification simply shows that the use of target capture in accordance with the invention **makes it possible** to use non-specific primers (i.e., non-specific amplification). Without target capture prior to amplification, non-specific amplification would not be a viable technique for detecting target nucleic acids in a sample because non-specific amplification causes the replication of virtually any nucleic acid sequence. However, this is not a problem because the invention of the '338 patent provides a target capture step that removes background, non-target nucleic acids from the sample prior to amplification. The specification does not state that one would not want to use specially tailored primers, but only that such primers are **not needed** in this invention. Thus, the specification simply discloses an important advantage of the invention, that is, because of the preceding target capture step, either specific or non-specific amplification can be successfully used

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(...continued)
parties' arguments regarding extrinsic evidence.

in nucleic acid detection assays; whereas without the invention, only specific amplification could be used.

The disclosure at column 30, lines 15-40 of the '338 patent specification tells those of ordinary skill in the art that, while the use of target capture made it possible to use non-specific amplification in assays for detecting nucleic acids, the invention was more generally directed to the use of target capture prior to any type of target amplification. The benefits of the invention, i.e., purifying the sample by removing non-target materials such as contaminants and inhibitors that can interfere with the amplification step, would also be obtained with specific amplification.[10] If the inventors had wanted to limit the invention to non-specific amplification, it is difficult to imagine that they would have drafted the specification as they did.

Indeed, Gen-Probe's earlier motion for summary judgment acknowledged the **permissive** rather than **mandatory** disclosure of the '338 patent specification regarding non-specific amplification:

> The inventors . . . pointed out that one of the express benefits of their invention was that it **permitted** the use of non-specific enzymes and non-specific primers.

(Memorandum of Points and Authorities in Support of Plaintiff Gen-Probe Incorporated's Motion for Partial Summary Judgment, filed April 30, 2001, at 11.)

Moreover, Example 5 of the '338 patent **does** explicitly disclose the use of a specific primer. In particular, while Example 5 states initially that random oligohexamer primers can be used to achieve non-specific amplification, Example 5 also discloses that "[a]lternatively, the double stranded DNA can be formed by synthesis starting from capture probe a." Col. 31, lines 48-49. In this instance, the capture probe acts as the primer. Since the capture probe binds specifically to the target DNA, the capture probe would be a specific primer to the target. This is an example of specific amplification because the primer, capture probe a, binds to a specific, unique DNA sequence in the target organism. (May 25, 2001 Persing Decl., ¶ 13.) Accordingly, the specification of the

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[10] This is precisely why Gen-Probe uses target capture before its TMA process. See Hill, "Gen-Probe Transcription-Mediated Amplification: System Principles" (Burwell Decl., Ex. A).

'338 patent demonstrates that specific amplification techniques are not "clearly excluded" from the literal scope of the claims.

B. The Prosecution History of the '338 Patent Demonstrates that Specific Amplification is Within the Scope of the Claims

The prosecution history of the '338 patent, the history of the correspondence between the patent owner and the PTO, leads to the inescapable conclusion that both the patent owner and the PTO (no fewer than five different Patent Office Examiners) considered the claimed invention to encompass the polymerase chain reaction ("PCR"), which is a type of specific amplification.

The initial application for the '338 patent included a broad claim (claim 1), which recited the step of "subjecting said removal product to amplification . . . ." (May 25, 2001 Declaration of Thomas W. Banks in Support of Vysis' Opposition to Gen-Probe's Motion for Partial Summary Judgment ("May 25, 2001 Banks Decl."), Ex. A, p. 61.)[11] In rejecting the claims of the original '338 patent application in the PTO's first Official Action, Patent Examiner Scott A. Chambers, Ph.D., and Primary Patent Examiner Amelia Burgess Yarbrough cited as prior art the basic Mullis PCR patents. (May 25, 2001 Banks Decl., Ex. B, pp. 3-4.) Clearly, if the Patent Examiners had believed that the claims of the '338 patent application were limited to non-specific amplification, it would have been illogical for them to have cited the PCR patents against the application, because PCR is a type of specific amplification. Thereafter, Examiner Chambers and Primary Examiner Margaret Moskowitz continued to cite the Mullis PCR patents against the pending patent claims. (May 25, 2001 Banks Decl., Ex. C, p. 3, and Ex. D, p. 3.)

In responding to rejections of the pending claims based on the Mullis PCR patents, the owner of the '338 patent never attempted to distinguish the Mullis patents by arguing that Mullis disclosed specific amplification, whereas the invention of the '338 patent was directed to non-specific

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[11] It is noteworthy in this regard that original dependent claim 11 contained language specifically further limiting the claim to "non-specific" amplification, which language was never incorporated into the broad claims. (May 25, 2001 Banks Decl., Ex. A.) The patent owner clearly knew how to exclude the disclosed use of specific amplification had it wanted to, but did not.

amplification. To the contrary, the patent owner repeatedly emphasized that the invention included PCR-type amplification:

> Applicant's invention principally serves to enhance the sensitivity of nucleic acid hybridization assays utilizing target amplification. **Targets can be amplified by a number of ways including PCR.** Applicant's invention enhances sensitivity by eliminating from the amplification medium extraneous (nonspecific) nucleic acids which might otherwise be amplified by PCR thereby introducing noise into the assay.

(May 25, 2001 Banks Decl., Ex. E, p. 18 (responding to November 5, 1992 Office Action in application serial no. 07/944,505) (emphasis added).)

If the patent owner had considered the invention to be limited to non-specific types of amplification, it undoubtedly would have argued this to the PTO to overcome the rejection of the patent claims based on the Mullis PCR patents, which disclosed specific amplification. Instead, the patent owner maintained all along that the invention encompassed PCR and argued that the invention was not obvious in view of the PCR patents. (May 25, 2001 Persing Decl., ¶ 16.)

The official recognition that the '338 patent claims encompassed specific amplification techniques like PCR persisted through the very end of the patent procurement process. Indeed, Patent Examiner Dianne Rees, Ph.D., and Primary Patent Examiner W. Gary Jones make it clear in the very first sentence of their Examiner's Statement of Reasons for Allowance that they considered the claims of the '338 patent to encompass specific amplification techniques such as PCR:

> The claims are drawn to methods of **PCR amplification** wherein the target is first separated from the sample by using a support that binds to the target polynucleotide and then amplified.

(May 25, 2001 Banks Decl., Ex. F, p. 2 (emphasis added).)

The only reasonable conclusion to be reached upon reading the prosecution history of the '338 patent is that both the patent owner and the five patent examiners who examined the patent application believed that the term "amplify" in the patent claims included specific amplification. (May 25, 2001 Persing Decl., ¶ 18.)

If the PTO's views from the original prosecution history were not enough, the PTO has adhered to these views in reissue proceedings. In its Protest to Vysis' reissue application for the '338 patent, Gen-Probe presented to the PTO the argument set forth in this motion that the

specification of the '338 patent does not provide a basis for claiming specific amplification after target capture. The PTO has indicated that it disagrees with Gen-Probe's interpretation of the '338 patent, stating in a January 16, 2001 Interview Summary that "the specification [of the '338 patent] provided basis for both specific and non-specific amplification of targets subsequent to capture." (May 25, 2001 Banks Decl., Ex. G, pp. 3-4.)

The Federal Circuit has made it clear that the Patent Examiner's understanding of the meaning of patent claims developed during prosecution is relevant to construing the proper scope and meaning of those terms. *Markman v. Westview Instruments, Inc.*, 52 F.3d. 967, 983 (Fed. Cir. 1995) ("It is evident from Markman's explanation of the claims to the examiner that he used 'inventory' in the patent and the examiner understood 'inventory' to consist of 'articles of clothing.'"); *Toro Co. v. White Consolidated Indus., Inc.*, 199 F.3d 1295, 1299 (Fed. Cir. 1999) ("Determining the limits of a patent claim requires understanding its terms in the context in which they were used by the inventor, considered by the examiner, and understood in the field of the invention.").

Federal District Courts, including this Court, have followed the Federal Circuit's direction and relied on the meaning of claim terms adopted by the PTO during patent prosecution in construing the meaning of patent claims. *Synthes v. Depuy Ace Medical Co.*, 1999 U.S. Dist. LEXIS 18173, *12-16 (E.D. Pa. 1999) (court declined to construe patent claim terms narrowly because Patent Examiner had rejected the claims based on prior art that met those terms only if construed broadly); *Sport Squeeze, Inc. v. Pro-Innovative Concepts, Inc.*, 51 U.S.P.Q.2d 1764, 1769 (S.D. Cal. 1999) ("the prosecution history of all three patents reveals that both [the inventor] and the patent examiner understood that differing particle sizes were significant in light of [the prior art]").[12]

Here, the case is even stronger than in *Synthes* for refusing the proffered narrow construction of the disputed claim language. The Patent Examiners of the '338 patent application rejected the claims in view of prior art disclosing the very embodiment, specific amplification, that Gen-Probe

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[12] The *Synthes* and *Sport Squeeze* cases are attached to the Notice of Lodgment of Case Authority Not In Official Reporter System in Support of Defendant Vysis' Opposition to Gen-Probe's Motion for Partial Summary Judgment, filed on May 25, 2001.

contends should not be included within the term "amplify." The patent owner, in response, explicitly acknowledged that the claims encompassed specific amplification techniques, such as PCR. Moreover, in the **very Reasons for Allowance** of the claims of the '338 patent, the PTO Examiners clearly stated their position that the claims included specific amplification, such as PCR.

The prosecution history of the '338 patent makes it clear that not only the patent owner but also the PTO considered specific amplification to be included within the claimed term "amplify." As the Federal Circuit observed in *Markman*, "[i]f the patent's claims are sufficiently unambiguous for the PTO, there should exist no factual ambiguity when those same claims are later construed by a court of law in an infringement action." *Markman*, 52 F.3d at 986.

C. The Cases Relied On By Gen-Probe Are Distinguishable

To support its argument that the doctrine of equivalents cannot cover a process encompassing an element that is clearly excluded from the literal terms of a claim, Gen-Probe primarily relies on *SciMed Life Systems, Inc. v. Advanced Cardiovascular Systems, Inc.*, 242 F.3d 1337 (Fed. Cir. 2001). In *SciMed*, the patent specification unequivocally described the embodiment of a **coaxial** lumen structure as the "basic sleeve structure for all embodiments of the present invention contemplated and disclosed herein." *SciMed* at 1339. The court added that "from the outset the specification identifies the inflation lumen, as that term is used in the SciMed patents, as annular, i.e., **coaxial** rather than **dual** in structure." *SciMed* at 1342 (emphasis added). Accordingly, the court limited the scope of the asserted claims to catheters with **coaxial** lumens and held that the patent disclaimed **dual** lumens. *SciMed* at 1340. In contrast to the '338 specification, the specification in *SciMed* used mandatory rather than permissive language making it clear that the invention **was** the use of coaxial lumens, not dual lumens. Also, unlike the present case, the specification in *SciMed* distinguished the invention from prior art that disclosed dual lumens and pointed out the advantages of coaxial lumens. *SciMed* at 1342-43.[13] Finally, unlike here, the court

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[13] As discussed above, though it had many opportunities to do so, the owner of the '338 patent never attempted to distinguish the invention of the '338 patent from the prior art by arguing that the invention of the '338 patent was directed solely to non-specific amplification.

noted that there was nothing pertinent to the issue of claim construction in the prosecution history. *SciMed* at 1340.

Similarly, in *Wang Laboratories, Inc. v. America Online, Inc.*, 197 F.3d 1377 (Fed. Cir. 1999), the patent specification always described the disputed term "frame" as being specific to "characters." Thus, the court concluded that the term included "character-based systems" but not "bit-mapped display systems." *Wang* at 1381. In contrast to *Wang*, the '338 patent specification clearly describes the embodiment of non-specific amplification in permissive and not mandatory language. Moreover, in *Wang*, unlike here, the only mention in the specification of the alternative embodiment ("bit-mapped display systems") was in the Background of the Invention, which the court viewed as simply an acknowledgement of the state of the art and not an enlargement of the invention. *Wang* at 1382. In contrast, here specific amplification is described in the description of the invention and the patent examples.

Finally, the prosecution history in *Wang* supported the limitation to character-based frames. During prosecution the patent applicant had distinguished prior art on the basis that it "encodes pictorial information . . . on the pel [picture element] level, rather than on the character level." *Wang* at 1384. Here, in contrast, the prosecution history makes it clear that the Patent Office (five different Patent Examiners) and the patent owner all considered the embodiment that Gen-Probe argues should be excluded from the claim, specific amplification, to be within the scope of the claimed invention. Accordingly, the argument that specific amplification techniques are "clearly excluded" from the claims of the '338 patent must fail.

In view of the foregoing, it could not be clearer that the PTO did not require the patent owner to, and the patent owner did not, surrender coverage of specific amplification processes in order to secure the '338 patent. To the contrary, everybody associated with the procurement of that patent, the PTO included, believed that specific amplification processes were covered by the patent. The "all elements" rule upon which Gen-Probe relies is intended to prevent patent owners who have succeeded in securing patents because they were limited in particular ways from vitiating those limitations through application of the doctrine of equivalents. The rule is also intended to give effect to the notice function of patent claims by allowing the public to rely on the scope of the patent grant

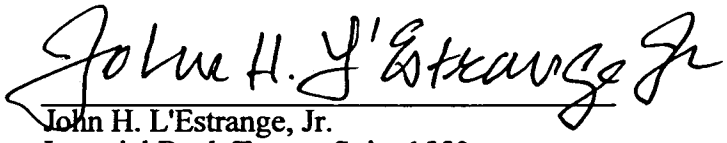
apparent from the face of the public prosecution record. Neither policy is offended here, where it could not be clearer in this case from the public record that everybody (the patent owner, the PTO, and Gen-Probe) viewed these claims as encompassing specific amplification. Indeed, the more disturbing result here would be that a limitation that does not appear in the claims at all, and that is in clear conflict with the prosecution history, should be read into the claim and then used to deprive the unsuspecting patent owner of access to the equitable protections afforded by the doctrine of equivalents on the ground that doing so would read the newly-imported limitation back out of the claim. There is no rule of law that would require the Court to do so in this case.

V. CONCLUSION

For the reasons pointed out herein, Gen-Probe's motion should be denied.

Date: October 30, 2001

WRIGHT & L'ESTRANGE



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UNITED STATES DISTRICT COURT

SOUTHERN DISTRICT OF CALIFORNIA

GEN-PROBE, INCORPORATED,

Plaintiff,

v.

VYSIS, INC.,

Defendant.

CASE NO.: 99CV 2668H (AJB)

CERTIFICATE OF SERVICE

CERTIFICATE OF SERVICE

I, the undersigned, declare under penalty of perjury that I am over the age of eighteen years and not a party to this action; my business address is 4665 Park Blvd., San Diego, California 92116; and that I served the below-named persons the following documents:

STIPULATION AND [PROPOSED] ORDER ALLOWING VYSIS, INCORPORATED TO FILE UNDER SEAL CERTAIN DOCUMENTS UPON WHICH IT RELIES IN OPPOSITION TO GEN-PROBE INCORPORATED'S MOTION FOR PARTIAL SUMMARY JUDGMENT OF NONINFINGEMENT UNDER THE DOCTRINE OF EQUIVALENTS

VYSIS' OPPOSITION TO GEN-PROBE'S MOTION FOR PARTIAL SUMMARY JUDGMENT OF NONINFRINGEMENT UNDER THE DOCTRINE OF EQUIVALENTS

VYSIS' STATEMENT OF DISPUTED FACTS IN OPPOSITION TO GEN-PROBE'S MOTION FOR PARTIAL SUMMARY JUDGMENT OF NONINFRINGEMENT UNDER THE DOCTRINE OF EQUIVALENTS

DECLARATION OF DAVID H. PERSING, PH.D., M.D. IN SUPPORT OF VYSIS' OPPOSITION TO GEN-PROBE INCORPORATED'S MOTION FOR PARTIAL SUMMARY JUDGMENT OF NONINFRINGEMENT UNDER THE DOCTRINE OF EQUIVALENTS

DECLARATION OF L. SCOTT BURWELL IN SUPPORT OF VYSIS' OPPOSITION TO GEN-PROBE INCORPORATED'S MOTION FOR PARTIAL SUMMARY JUDGMENT OF NONINFRINGEMENT UNDER THE DOCTRINE OF EQUIVALENTS

NOTICE OF LODGMENT OF CASE AUTHORITY NOT IN OFFICIAL REPORTER SYSTEM IN SUPPORT OF VYSIS' OPPOSITION TO GEN-PROBE INCORPORATED'S MOTION FOR PARTIAL SUMMARY JUDGMENT OF NONINFRINGEMENT UNDER THE DOCTRINE OF EQUIVALENTS

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Executed on October 30, 2001, at San Diego, California.

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